54651

TSCA HEALTH & SAFETY STUDY COVER SHEET

TSCA CBI STATUS: NONE

8EHQ-0102-15065

RECEIVED OPPT CBIC

2002 JAN 28 AM 6:50

1.0 SUBMISSION TYPE

8(d) **XX 8(e)** FYI 4 OTHER: Specify_____

XX- Initial Submission - Follow-up Submission Final Report Submission

Previous EPA Submission Number or Title if update or follow-up: Docket Number, if any: #

continuation sheet attached

2.1 SUMMARY/ABSTRACT ATTACHED (may be required for 8(e): optional for §4, 8(d) & FYI)	**2.2 SUBMITTER TRACKING NUMBER OR INTERNAL ID**	**2.3 FOR EPA USE ONLY**
X- YES NO	**7106 4575 1292 0337 7937** **01-2-38**	

3.0 CHEMICAL/TEST SUBSTANCE IDENTITY

Reported Chemical Name (specify nomenclature if other than CAS name):

CAS# N/A

Purity ___%

Contain NO CBI

X- Single Ingredient

Commercial/Tech Grade

Mixture *Trade Name:* AMS 21618 *Common Name*: Strobilurin

CAS Number	*NAME*	*% WEIGHT*

Other chemical(s) present in tested mixture

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4.0 REPORT/STUDY TITLE

Evaluation of A Chronic Toxicity Study in the Beagle Dog, Report # 110920

continuation sheet attached

5.1 STUDY/TSCATS INDEXING TERMS

[CHECK ONE]

HEALTH EFFECTS (HE):__X___ ENVIRONMENTAL EFFECTS (EE):_____ ENVIRONMENTAL FATE (EF):_____

5.2 STUDY/TSCATS INDEXING TERMS (see instructions for 4 digit codes)

STUDY TYPE: _CTOX	SUBJECT ORGANISM (HE, EE only) _DOGS	ROUTE OF EXPOSURE (HE only):__	VEHICLE OF EXPOSURE (HE only)_
Other:	*Other:*	*Other:*	*Other:*

6.0 REPORT/STUDY INFORMATION Study is GLP

Laboratory Bayer Toxicology Report/Study Date 12/20/01

Source of Data/Study Sponsor (if different than submitter) _____ Number of pages _-

continuation sheet attached

7.0 SUBMITTER INFORMATION

Janet M. Mostowy, Ph.D.
VP, Product Safety & Regulatory Affairs Phone: 412-777-3490
Bayer Corporation - 100 Bayer Road, Pittsburgh, PA. 15205

Technical Contact: **SAME AS ABOVE** Phone: ( )_____

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8.0 ADDITIONAL/OPTIONAL STUDY COMMENTS

This compound is a developmental pesticide.

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Submitter Signature: _____ **Date: 12/20/01**

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Continuation of 2.1

The reporting of results for chronic studies requires indications of carcinogenicity, neurotoxicity, or irreversible degenerative changes to any organ or organ system of a potentially serious nature. Thus reporting based on the renal tubular degeneration/swelling in one dog in the high-dose group.

Summary

Technical grade AMS 21618 was administered in the diet to Beagle dogs (4 animals per sex and treatment level) at nominal concentrations of 0, 25, 50, 250, and 1,200 ppm of technical grade AMS 21618 mixed in the feed on the basis of the active ingredient. The purpose of this study was to characterize the general toxicity, resulting from a one-year duration, continuous per *os* exposure of the Beagle dog to technical grade AMS 21618. In addition to the routine guideline requirements, this study investigated potential cardiac and neurologic effects. Computerized electrocardiography (ECG) measurements were performed after approximately 90 days. Neurological examinations were performed prior to treatment and necropsy which included peripheral and cranial reflex tests, task performance tests, gait, and behavioral observations.

There was a compound-related decrease in food consumption in the high-dose males and females. There was a compound-related decrease in body weight (growth rate) in the mid-dose (250 ppm) females and high-dose males and females. There were no clinical observations or ophthalmology findings in this study that were considered to be compound-related. Likewise, there were no compound-related changes found in the ECG parameters measured in this study. Neurologic examination, thoracic auscultation, and rectal body temperatures were all within normal limits.

The following summarizes the clinical, gross and microscopic pathology compound-related findings:

1. There were alterations in the following clinical pathology parameters:
   (a) ALT and GGT were significantly increased in a biologically relevant manner in the 1,200 ppm dose group for both sexes.

   (b) ALP was significantly increased in a biologically relevant manner in the 250 and 1,200 ppm dose group for both sexes.

   (c) TProt and ALB were significantly decreased in a biologically relevant manner in the 1,200 ppm dogs dose group for both sexes.

2. There was a compound-related, significant increase, in relative hepatic weights for males and females in the 1,200 ppm dose group.

3. The following morphologic alterations were considered to be compound-related:
   (a) Hepatocyte enlargement (hepatocytomegaly) was increased in males and females in the 250 and 1,200 ppm dose groups.

   (b) Renal pigmentation was increased in males and females in the 1,200 ppm dose group. One instance of renal tubular degeneration/swelling in a male in the 1,200 ppm dose group was attributed to treatment.

This chronic feeding study with technical grade AMS 21618 demonstrated a NOAEL (no--observed-adverse-effect level) in both sexes at 50 ppm. An intermediate level of toxicity was seen at 250 ppm, based on liver findings and decreased body weights in females. The MTD (maximum-tolerated-dose) was considered to be 1,200 ppm, within the limits of animal welfare concerns, based on the hepatic and renal pathology changes. The target organs of toxicity appeared to be the liver and kidney.